

CLAIMS

1. A method for producing a biochip including a support on which is immobilised a set of polynucleotides, characterised in that it includes :

- 5 (i) obtaining BAC clones including a nucleic insert corresponding to or specific to a portion of a human genome,
- (ii) selecting, from the BAC clones thus obtained, a set of BAC clones including a single nucleic insert in the human genome, the BAC clones of the selected set including nucleic inserts substantially uniformly
- 10 distributed over the human genome, this selection step including :
- (a) eliminating non-single clones ;
- (b) eliminating clones sharing a same STS ;
- (c) eliminating STS which are marked at at least two different places on the human genome ;
- 15 (d) classifying clones as a function of their position on the genome, thus defining neighbouring clones ; and
- (e) additionally eliminating clones, by applying an iterative method, so as to obtain in particular substantially uniform distribution over the human genome of the finally selected clones; and
- 20 (iii) depositing, on a support, clones thus selected, or the nucleic inserts that they contain, or part of them, in conditions enabling the deposited clones or inserts to hybridise with a nucleic acid having a complementary sequence.

- 25 2. The method according to claim 1, characterised in that step (i) includes obtaining a collection of BAC clones including nucleic inserts likely to cover the whole sequence of the human genome.

3. The method according to claim 1 or 2, characterised in that the BAC clones of the selected set include nucleic inserts spaced apart from one another by an interval of an order of about 1Mb.
- 5 4. The method according to any of claims 1 to 3, characterised in that selection steps a) to e), or part of them, are repeated at least once until a set of BAC clones is obtained including a single insert in the human genome, the BAC clones of the selected set furthermore including nucleic inserts substantially uniformly distributed over the human genome, and covering the whole human genome.
- 10 5. The method according to any of claims 1 to 4, characterised in that step a) is implemented by compilation or analysis of the information known for a clone (positioning, marker, sequence, etc...), by computer analysis of the sequence of the nucleic insert that they contain and/or by biological experiments.
- 15 6. The method according to any of claims 1 to 5, characterised in that step e) comprises a first sub-step e_1) of extracting, by means of a first criterion, a sub-set of BAC clones likely to be eliminated from the finally selected set of clones, and a second sub-step e_2), during which a second criterion is applied to the elements
- 20 of the sub-set of clones likely to be eliminated, so as to determine the single clone of this sub-set which will be effectively eliminated.
7. The method according to claim 6, characterised in that the first sub-step e_1) of extracting from the sub-set BAC clones likely to be eliminated is implemented by
- 25 applying a first rejection criterion based upon the calculation of a variance between neighbouring BAC clones, in particular a criterion defining a maximum authorised distance between two neighbouring clones of the finally selected set of clones.

8. The method according to claim 6 or 7, characterised in that the second criterion applied during the second sub-step e₂) includes requiring a minimum distance between two neighbouring clones of the finally selected set of clones.
- 5 9. The method according to claim 7 or 8, characterised in that the first criterion is based upon a maximum distance of 1.5 Mb and the second criterion includes requiring a minimum distance of 0.7 Mb.
- 10 10. The method according to any of the preceding claims, characterised in that step (ii) of selecting BAC clones is implemented by means of a computer programme.
- 15 11. The method according to any of the preceding claims, characterised in that, in step (iii), the BAC clones or the nucleic inserts that they contain, or part of these clones or inserts, are deposited on a support by direct coupling on the support, or by an interaction with a complementary oligonucleotide, or by means of a spacer arm.
- 20 12. The method according to claim 11, characterised in that the support is level and/or rigid.
- 25 13. The method according to claim 11 or 12, characterised in that the support is made with a base of materials chosen from glass, plastic, polymer, metal, biological materials, silicones and nylon.
14. The method according to claim 13, characterised in that the support is a glass slide.

15. The method according to any of the preceding claims, characterised in that, during step (iii), depositing is implemented according to a (pre)-specified arrangement and/or density.
- 5 16. The method according to any of the preceding claims, characterised in that, prior to step (iii), the clones of the selected set are sub-cultured, amplified, characterised and/or stored.
- 10 17. The method for producing a biochip including a support on which has been immobilised a set of polynucleotides, characterised in that it includes :
- (i) obtaining BAC clones including a nucleic insert corresponding to or specific to a portion of a human genome ;
 - (ii) selecting, from the BAC clones thus obtained, a set of BAC clones including a single insert in the human genome, BAC clones of the selected set
15 including nucleic inserts substantially uniformly distributed over the human genome, this selection step including :
 - (a) eliminating non-single clones ;
 - (b) eliminating clones sharing a same STS ;
 - (c) eliminating STS which are marked at at least two different places
20 on the human genome ;
 - (d) classifying clones as a function of their position on the genome, thus defining neighbouring clones ; and
 - (e) additionally eliminating clones, by applying an iterative method, so as to obtain in particular substantially uniform distribution over the
25 human genome of the finally selected clones ;
 - (iii) amplifying the BAC clones of the selected set and/or the nucleic inserts that they contain ; and
 - (iv) depositing, on a support, clones selected in this way or the nucleic
30 inserts that they contain, or part of them, in conditions enabling deposited clones or inserts to hybridise with a nucleic acid having a complementary sequence.

18. A biochip, characterised in that it includes a support on which is immobilised a set of BAC clones including a nucleic insert corresponding to or specific to a portion of a human genome, each clone including a single insert in the human genome and carrying an STS not shared by any other insert of the BAC clones of the set, the BAC clones of the set including nucleic inserts substantially uniformly distributed over the human genome.

19. The use of a biochip according to claim 18 for identifying genes, for genetic mapping, for diagnosis or in pharmacogenomics.

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20. A method for identifying or locating a nucleic acid on the human genome, including placing a nucleic acid in contact with a biochip according to claim 18, in conditions enabling hybridisation between complementary sequences, detection of a hybridisation signal, and identification of the position of the nucleic acid on the genome by identification of the clones involved in the hybridisations.

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21. A method for identifying genes associated with a given character trait, including (i) identifying fragments of nucleic acids identical between at least two samples taken from subjects having a common character trait, and (ii) hybridising fragments thus identified on a biochip according to claim 18 and, (iii) detecting a hybridisation signal, making it possible to locate the fragment(s) on the human genome and thus to identify one or more genes present therein, associated with said character trait.

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